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Reversed-phase liquid chromatographic determination of isoniazide in human urine as a test of the genetically predetermined type of biotransformation by acetylation

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Abstract

A new method of determination of genetically predetermined type of biotransformation by acetylation rate using reversed-phase liquid chromatography (RP-HPLC) was described. The method is based on determination of isonicotinic hydrazide (INH) which is excreted with the patient's urine during 24 h period after oral administration of 0.4 g of the drug. INH is used as pharmacogenetic marker. Precolumn derivatization of 4-chloro-5,7-dinitrobenzofurazan is used at RP-HPLC determination of INH and a new drug phosphabenzide (diphenylphosphinylacetic hydrazide, DPPAH) with specrtophotometric detection in urine. The limit of INH detection was 0.27 μg ml^{-1} and the one of DPPAH was 0.82 μg ml^{-1}. As a result of pharmacokinetic investigation it was discovered that bimodal distribution by acetylation rate for DPPAH is less apparent than in the case of INH. It is shown, that immunomodulator xymedone (*N*-(β-oxyethyl)-4,6-dimethyldihydropirimidon-2) is the acetylation inductor of xenobiotics.

Keywords: RP-HPLC; Derivatization; 4-Chloro-5,7-dinitrobenzofurazan; Drugs

1. Introduction

Clarification of the connection between concentration of xenobiotics, their metabolites and pharmacological effect is the base of effective and secure application of drugs as well as diagnostics and treatment of personnel exposed to industrial toxicants [1–4]. In connection with this, the task of the development of sensitive and selective methods of determination of drugs and other xenobiotics in biological substrates of a human being is very urgent. The availability of relatively simple and clinically applicable methods for the determination of drugs in biological substrates for diagnostics of genetically predetermined type of

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